Attorney Docket No. 9022-41 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Maurer et al.
Application Serial No.: 10/767,352
Filed: January 30, 2004
Confirmation No.: 4884
Group Art Unit: 1618
Examiner: Blessing M. Fubara
For: *Oral Compositions of Fenretinide Having Increased Bioavailability and Methods of Using the Same*

Date: April 14, 2010

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REMARKS ACCOMPANYING DECLARATION UNDER 37 C.F.R § 1.132 OF BARRY J. MAURER, MD, PhD

Sir/Madam:

The attached Declaration Under 37 C.F.R.§ 1.132 of Dr. Barry J. Maurer, MD, PhD ("Rule 132 Declaration") is submitted herewith in response to the Examiner's request. This Rule 132 Declaration is substantially similar to the Declaration Under 37 C.F.R.§ 1.132 of Dr. Barry J. Maurer, MD, PhD submitted on January 27, 2010. Accordingly, the attachments/exhibits are not submitted herewith.

Applicants respectfully submit that the present application is in condition for allowance and the same is earnestly solicited. The Examiner is encouraged to telephone the undersigned at 919-854-1400 for resolution of any outstanding issues.

Respectfully submitted,

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CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on April 14, 2010.

Betty-Lou Rosser

Attorney Docket No. 9022-41 PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

April 13, 2010

Commissioner for Patents
Post Office Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R § 1.132
OF BARRY J. MAURER, MD, PhD

Sir/Madam:

I, Barry J. Maurer, MD, PhD, do hereby declare and say as follows:

1. I received my PhD from California Institute of Technology. I received my medical degree from Wayne State University. I completed an internship at Children's Hospital of Michigan and a residency at LAC/USC Pediatric Pavillion in Los Angeles, CA. I also completed a clinical fellowship in pediatric oncology at Fred Hutchison Cancer Research Center and a research fellowship at Childrens Hospital Los Angeles Research Institute. I am further certified by the American Board of Pediatrics in hematology/oncology. I am currently an Associate Professor of Cell Biology, Pediatrics, and Internal Medicine at Texas Tech University Health Sciences Center in Lubbock, TX.

2. I am a co-inventor listed on U.S. Patent Application Serial No. 10/767,352 (hereinafter, "the '352 application"). I have reviewed the Office Action dated October 27, 2009 issued in association with the '352 application, and I am familiar with the contents

thereof. I have also reviewed U.S. Patent No. 6,352,844 to Maurer et al. (of which I am a co-inventor); U.S. Patent No. 4,874,795 to Yesair; U.S. Patent No. 5,972,911 to Yesair; and U.S. Patent No. 4,665,098 to Gibbs, all of which are cited in the Office Action.

3. My efforts are dedicated to development of new drugs for use against childhood cancers. In particular, neuroblastoma, a type of cancer that affects the nervous system, typically occurs in children under 10 years of age. The previous (and largely ineffective) daily dosage of fenretinide, a synthetic vitamin A derivative, to treat this disease was 60 to 70 hard, oversized capsules. My colleagues and I knew we had to develop something better. Being pediatricians, we know that getting kids to take medicine is a challenge. We have now shown that fenretinide can not only be provided in a more palatable and more convenient way for patients, it can finally be absorbed into the blood at levels capable of shrinking tumors. Additionally, this fenretinide composition can be provided to patients with relapsed neuroblastoma and achieves higher plasma levels than equivalent fenretinide doses previously delivered using corn oil capsules. This new formulation can be further provided with minimal toxicity.

4. We hypothesized that fenretinide/LYM-X-Sorb^{TM} (LXS) oral powder would increase fenretinide plasma levels in relapsed neuroblastoma patients compared to the previously tested fenretinide/corn oil capsule thereby increasing drug delivery to the tumor bed and improving antitumor responses and further facilitating patient compliance with drug administration as compared to the corn oil capsules of conventional fenretinide formulations. Accordingly, a phase I trial in recurrent/resistant neuroblastoma was conducted using a dosing schedule of seven consecutive days of fenretinide/LXS oral powder, every three weeks. Methods are described in greater detail at **Appendix 1**.

5. As shown in the figure provided at **Appendix 2**, results of this study showed that fenretinide/LXS oral powder attained several-fold higher fenretinide plasma levels (peak and trough) compared to equivalent doses of fenretinide previously delivered using corn oil capsules on similar dosing schedules. Additionally, the increased

fenretinide plasma levels did not appreciably increase observed side effects (as noted in Tables 1 and 2 at **Appendix 3**) compared to those reported with conventional high dose oral capsule fenretinide treatment such as reversible liver dysfunction, hypertriglyceridemia, idiosyncratic pseudotumor cerebri, nausea and mild thrombocytopenia. In this study, the most significant side effect was moderate, reversible liver toxicity with minimal hematopoietic side effects as shown in Table 3 of **Appendix 3**.

Of further clinical significance, the fenretinide/LXS oral powder scored more Complete Responses (%) in neuroblastoma tumor than when using the corn oil capsules as shown in the table at **Appendix 4**. Thus, we have demonstrated that obtaining higher drug levels in the blood plasma can, in fact, lead to a better anticancer treatment effect.

6. In summary, the formulations described in the '352 application provide a new formulation for the delivery of fenretinide that yields positive results including increased plasma concentrations. The formulations described in the '352 application represent a new treatment for a childhood cancer that was difficult to treat as well as a new treatment modality for other diseases in which fenretinide may represent a treatment option.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Barry J. Maurer, MD, PhD

4/13/10
Date